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PUBLIC HEALTH SERVICE

IN REPLYING, ADDRESS THE

Tuberculosis Research Laboratory,
411 East 69th St., New York 21, N. Y.

May 21, 1951.

Dr. Joshua Lederberg,
Department of Genetics,
The University of Wisconsin,
College of Agriculture,
Madison 6, Wisconsin.

Dear Joshua:

Thanks very much for your letter of May 15th and your description of your "microbial printing press". Combined with a photo-reactivation method of developing the pattern designed for reproduction, I can see that this technique might be the beginning of a major development in the age of bio-technology that Julian Huxley has predicted as the next great development in science!

In all seriousness, it sounds like a good trick, and I can't think off-hand of any improvement. I hope you can get somebody to try out the application of drug resistance that you describe. I am grateful to you for suggesting it but am too preoccupied with various metabolic problems to undertake this study myself. Off-hand, I would think this method very useful for the screening of drug resistant, auxotrophic, and similar colonies, but in linkage studies I wonder whether there might not be grave danger of falsely identifying a marker because of the variable density of the transfers to the successive plates, which might affect the response to tests for fermentation or growth requirement.

I am planning to go to a good part of the Cold Spring Harbor meetings and look forward to seeing you there. I've urged Harry Eagle to take in the microbiological portion, for I think that he could both gain and contribute a good deal by more extensive contact with microbial genetics. My attitude toward his revolutionary conclusions has remained pretty conservative; I'll be interested to learn how you react to his material.

While most of our stuff has been straight biochemistry this year, I have recently picked up some evidence for qualitatively altered enzymes as the mechanism underlying drug resistance. Briefly, this consists in finding that p-nitrobenzoic acid is a simultaneous competitor of PABA and POB; resistance to PABA develops separately with each of these two systems, eliminating permeability as an explanation. In addition,

resistance to this competitor, substituted at the 4 position of the two metabolites, is independent of resistance to other competitors substituted at the carboxyl (1) position. This last observation seems to exclude a good many possible mechanisms, such as increased production of a metabolite, increased amount of enzyme utilizing it, or increased efficiency in utilizing the product of this enzyme. We don't have much stuff so far, but perhaps there will be enough for a discussion at the Symposium.

See you soon.

Sincerely yours,

Bernie H.L.

Bernard D. Davis

BDD/hl